Case Reports

Primary Malignant Mesothelioma of the Pericardium

Case Report and Literature Review

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Pericardial mesothelioma is a highly lethal and fortunately rare cardiac neoplasm. We present the clinical and pathologic features of a primary sarcomatoid mesothelioma. To better understand the clinical, radiographic, and pathologic features of this entity, we reviewed 27 cases described in the English literature from 1972 through 1992, which, together with our case, provided a total of 28 cases. Findings of the review include a male-female ratio of 2:1, a wide age range (12 to 77 years; mean, 47 years), and documented asbestos exposure in 4 of 28 (14%) patients. Commonly used imaging studies do not appear to offer great sensitivity, for a mass was detected by echocardiography in only 2 of 16 (12%) patients and by computed tomography in 4 of 9 (44%). Pathologic findings revealed a diffuse growth pattern in most cases (18 of 25, or 72%), together with an equal distribution between the biphasic, epithelioid, and sarcomatoid variants. Effusion cytology revealed malignant cells in only 2 of 10 (20%) cases. With or without therapy, prognosis was uniformly poor, since 24 of 27 patients were dead of the disease at the time the reports were published. ***(Texas Heart Institute Journal 1994;21: 170-4)***

Key words: *Asbestos; cardiac tamponade; heart neoplasms; heart surgery; immunohistochemistry; mesothelioma/pathology; myocardial infarction; pericardial effusion; pericardium*

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Pericardial mesothelioma is a rare and highly lethal cardiac tumor. There has been no organized review of diagnostic criteria, treatment, or outcome in the English literature for over 20 years. We consider patient clinical characteristics, diagnostic criteria, and the usefulness of various diagnostic methods, within the context of a literature review and discussion of a case.

Case Report

Clinical History. The patient, a 36-year-old woman, developed dyspnea, cough, low-grade fever, and night sweats approximately 4 months prior to admission. Initially, she was evaluated at a hospital in another city, without a firm diagnosis. Due to progressive symptoms and the development of nausea and vomiting, along with lower-extremity edema, she presented at our hospital in October of 1992. Previous medical history was noncontributory.

The physical examination at admission demonstrated signs of pericardial tamponade. Chest radiography revealed marked enlargement of the cardiac silhouette. Echocardiography demonstrated a large pericardial effusion, with echocardiographic signs of tamponade. A pericardial window was promptly placed via a subcostal approach. Intraoperative digital exploration of the pericardial space was unremarkable. The removal of effusion fluid resulted in marked relief of tamponade symptoms. Specimens of bloody pericardial fluid and a section of pericardium were negative for malignancy by cytologic and histologic examination, respectively. In addition, cultures and smears (bacteria, acid-fast bacilli, and fungi) were negative. Sections of the pericardium showed non-caseating granulomas. The presumptive diagnosis of an infectious process was made; while awaiting culture results, antibiotic therapy was initiated as recommended by infectious disease consultants.

One week after pericardial window placement, a repeat echocardiogram demonstrated reaccumulation of the pericardial fluid and a mass behind the left ventricle. There were no clinical or echocardiographic signs of recurrent tamponade.

For biopsy of the mass, the patient was advised to undergo a repeat pericardial window procedure via a thoracotomy. She refused.

The 2nd admission, 3 weeks after the 1st, revealed an apparently ill patient with a blood pressure of 112/70, a pulse rate of 108, a respiratory rate of 20, and a temperature of 99 °F. Examination was otherwise notable for estimated right atrial pressures of 12 cm H_2O, no Kussmaul's sign, and no pulsus paradoxus. Upon auscultation, the left hemithorax was dull to percussion, with bibasilar crackles; the point of maximal impulse was diffuse, an S_4 was present, but there was no S_3, no rub, and no knock. Marked hepatomegaly and 3+ pedal edema were present. Repeat echocardiography showed expansion of the pericardial effusion, no echocardiographic signs of tamponade, and an increase in size of the previously noted retrocardiac mass. Computed tomographic scans of the chest (Fig. 1) and abdomen demonstrated bilateral pleural effusions, homogeneous hepatomegaly, and a large pericardial effusion. A mass was noted to be attached to the posterior aspect of the left ventricle, to the left atrium, and to the mediastinal structures superior to the left atrium. There was minimal lymphadenopathy.

Sternotomy was performed, and digital exploration of the pericardial space revealed a tumor encasing the heart. There was initial recovery followed by sudden intractable cardiac arrest, with electromechanical dissociation.

Postmortem Examination. The heart revealed diffuse involvement of the epicardium by a gray-white fleshy tumor having a maximal thickness of 5 cm at the base of the heart. In general, there was a distinct border between the tumor and the underlying myocardium, but areas of obvious myocardial infiltration were observed, most notably at the posterior basal segment of the left ventricle, where myocardium was essentially replaced by tumor (Fig. 2). Tumor packed the pericardial sleeve, investing the roots of the aorta and main pulmonary artery. Within the mediastinum, the tumor was confined by the parietal pericardium. Metastases were noted in the lung, with 4 subpleural nodules ranging up to 1.5 cm in maximum dimension. An organizing thrombus was present within the right atrium, and 2 recent infarcts were noted in the lungs. Acute emboli were present throughout large pulmonary artery branches within the lung parenchyma.

Histopathologic Findings. The general histologic appearance of the tumor consisted of variably sized nodules containing sheets of uniform spindle cells with scanty-to-moderate amounts of eosinophilic cytoplasm and with fusiform-to-oval nuclei having marginated chromatin and inconspicuous nucleoli (Fig. 3). A smaller component of tumor contained cohesive round-to-oval epithelioid cells. Definitive acinar, tubular, or papillary structures were not ob-

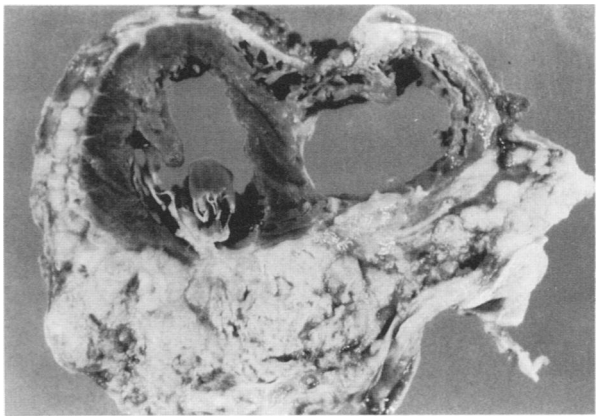

Fig. 2 *Gross pathologic specimen of the heart at the papillary muscle level. The tumor essentially encases the heart. Myocardium is infiltrated and replaced at the base of the heart.*

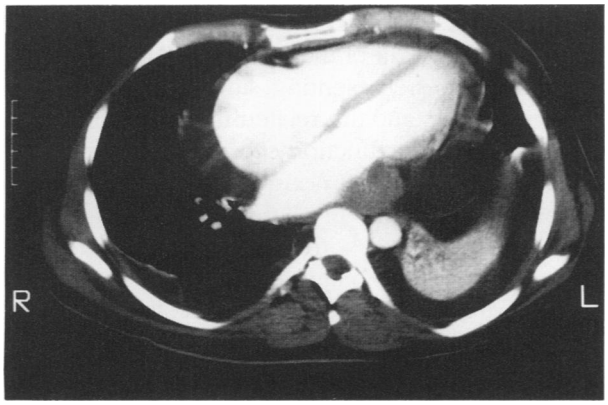

Fig. 1 *Computerized tomographic image of the chest, with contrast. The retrocardiac mass at the level of the atrioventricular groove is well visualized, as is the pericardial effusion. There is also a pleural effusion, and the right atrium appears enlarged.*

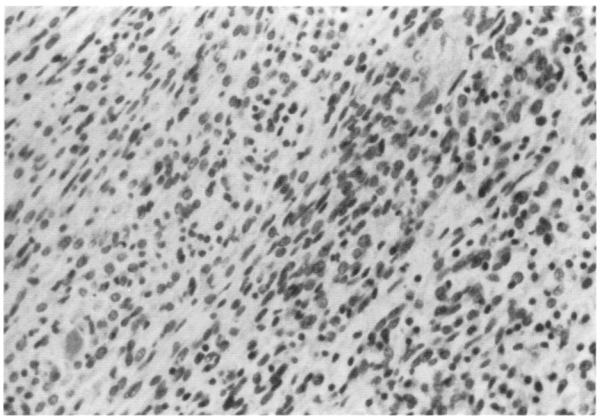

Fig. 3 *Photomicrograph illustrating parallel fascicles of relatively bland oval and spindle cells. (H + E, orig. x400)*

served. The mitotic index varied with location, but areas containing greater than 5 mitoses per 10 high-power fields were present.

Immunohistochemical studies revealed strong vimentin positivity in virtually all tumor cells. Less than 1% of tumor cells demonstrated strong staining for cytokeratin. The remainder of the immunostain battery, including S100, myoglobin, desmin, actin, epithelial membrane antigen, B72.3, and synaptophysin, was negative.

Electron microscopy displayed spindled and oval cells containing generally scanty amounts of rough endoplasmic reticulum, Golgi material, and mitochondria (Fig. 4). The cytoplasmic contours were smooth. Occasional cells contained discontinuous basal lamina material. Primitive cell junctions were observed between clustered oval cells. Although intermediate filaments were quite prominent, neither microfilaments nor microvilli were observed.

Interpretation of Pathologic Findings. The tumor's location and gross pattern of growth, i.e., mostly within the pericardium and forming a rind over the epicardial surface, suggested a diagnosis of mesothelioma. The histologic findings were consistent with the sarcomatoid variant of mesothelioma. However, the relatively undifferentiated spindle cell pattern merited the consideration of sarcomas such as malignant peripheral nerve sheath tumor, leiomyosarcoma, fibrosarcoma, and rhabdomyosarcoma, all of which have been reported as primary cardiac tumors.[1] The biphasic immunostain positivity for vimentin and cytokeratin supported a diagnosis of sarcomatoid mesothelioma. This is the typical pattern displayed by the sarcomatoid and other variants of malignant mesothelioma.[2-5] Most cases of sarcomatoid mesothelioma display positive staining for cytokeratin in >50% of tumor cells, while a smaller number of cases have been reported to display only focal positivity.[5-7] Rare cases are reported to be cytokeratin negative.[3,4] The results of the immunostain battery did not support a nerve sheath, smooth or striated muscle, or fibroblast origin. The ultrastructural features of 10 cases of sarcomatoid mesothelioma were studied by Klima and Bossart,[7] whose findings support a diagnosis of malignant mesothelioma in our tumor, due to the presence of basal lamina material and primitive cell junctions. Microvilli are a prominent ultrastructural finding in the epithelioid and biphasic variants of mesothelioma. However, Klima reported that 5 of their 10 study cases of sarcomatoid mesothelioma revealed no microvilli. Such an absence was observed in our case. The ultrastructural findings were not supportive of alternative diagnoses in the differential diagnosis. Taken together, the pathologic studies provided a definitive diagnosis of primary pericardial sarcomatoid mesothelioma.

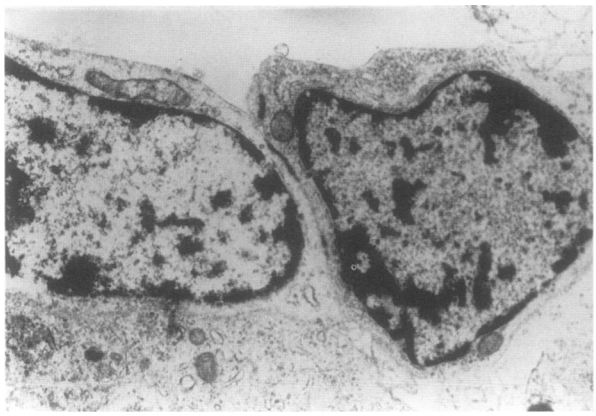

Fig. 4 *Electron micrograph illustrating discontinuous basal lamina and primitive cell junctions. (orig. x26,000)*

Discussion and Literature Review

Pericardial mesothelioma is a rare tumor constituting approximately 4% of the primary heart and pericardial tumors in the Armed Forces Institute of Pathology series[1] and 1% of malignant mesotheliomas in a registry of 180 patients by the Dana Farber Cancer Institute and Brigham and Women's Hospital.[8] The last extensive review of the entity was undertaken in 1971 by Sytman and MacAlpin.[9] In order to update the available knowledge concerning its clinical and pathological features, we reviewed 24 literature citations of 27 cases in which a diagnosis of primary pericardial mesothelioma was made.[10-33] These citations appeared in the English literature from 1972 through 1992. The findings of this review, combined with the findings in our case, are summarized in Tables I-IV.

Table I illustrates that for the 28 cases, there is a male–female ratio of 2:1. Although a wide age range is affected, over half of the cases occur in the 5th to the 7th decades. Presenting signs and symptoms are nonspecific, and are related mostly to the compromise of cardiac function caused by tumor mass, effusion, or both. This nonspecificity may lead to diagnostic consideration or treatment of other disease states associated with pericardial effusion, such as rheumatic fever,[15] metastatic disease,[20] dissecting aortic aneurysm,[15] viral syndrome,[20] collagen vascular disease,[11,21,25] and tuberculosis.[31] Due to extension of tumor into the myocardium and cardiac chambers, acute myocardial infarction or cerebral vascular accident may occur during the course of the disease.[17,21,33] The role of asbestos exposure as a causative factor in the development of pericardial mesothelioma is not certain, but asbestos exposure has been documented in a few patients.[16,18,34]

TABLE I. Reported Characteristics and Presenting Symptoms of Patients*

Sex	
Male	20/28 (71%)
Female	8/28 (29%)
Age	
Range	12-77 years
Median	48 years
Mean	47 years
Most Commonly Cited Presenting Symptoms	
Dyspnea	13/28 (46%)
Fever	9/28 (32%)
Chest pain	9/28 (32%)
Weight loss	6/28 (21%)
Asbestos Exposure	
Not mentioned	16/28 (57%)
Exposure	4/12 (33%)
No known exposure	8/12 (67%)

*Drawn from references 10 through 33 and the present case.

TABLE II. Summary of Reported Radiographic Findings in Pericardial Mesothelioma*

Chest Radiography	
Results not available	4/28 (14%)
Results available	24/28 (86%)
Normal	4/24 (17%)
Enlarged cardiac silhouette	16/24 (67%)
Mediastinal widening	1/24 (4%)
Anterior mediastinal mass	1/24 (4%)
Echocardiography	
Not done or results not available	12/28 (43%)
Results available	16/28 (57%)
Effusion	14/16 (88%)
Tamponade	3/16 (19%)
Thickened pericardium	3/16 (19%)
Mitral valve abnormality	2/16 (12%)
Pericardial mass	2/16 (12%)
Pericardial cysts instead of mass	1/16 (6%)
Pericardial adhesions instead of mass	1/16 (6%)
Computed Tomography	
Not done or results not available	19/28 (68%)
Results available	9/28 (32%)
Pericardial mass	4/9 (44%)

*Drawn from references 10 through 33 and the present case.

TABLE III. Summary of Pathologic Findings*

Gross Findings	
Diffuse growth	18/25 (72%)
Discrete mass(es)	7/25 (28%)
Not available	3/28 (11%)
Myocardial invasion	18/28 (64%)
Extra-mediastinal metastases	7/28 (25%)
Effusion Cytologic Findings	
Not available	18/28 (64%)
Benign	7/10 (70%)
Inconclusive	1/10 (10%)
Malignant	2/10 (20%)
Histopathologic Findings	
Not available	8/28 (28%)
Biphasic	7/20 (35%)
Epithelioid	7/20 (35%)
Sarcomatous	6/20 (30%)

*Drawn from references 10 through 33 and the present case.

Although chest radiography and echocardiography are sensitive means of detecting enlarged cardiac silhouette and effusion, Table II illustrates that they lack sensitivity in detection of pericardial mesothelioma. This likely is due to the tendency of this tumor to exhibit a diffuse growth pattern (Table III) in which tumor envelopes the heart, rather than a pattern of growth as a discrete mass. Computed tomography appears to offer a greater sensitivity for detection of the tumor.[15,20,22,25,35] In the 2 reports in which it was mentioned, magnetic resonance imaging successfully identified tumor.[22,27] Finally, radionuclide imaging (with radiogallium) was reported to have been of assistance in the detection of tumor in 2 cases.[22,25]

Table III summarizes the pathologic findings of the cases. A diffuse growth pattern is most common, and myocardial invasion is not uncommon. Involvement of the mitral valve resulting in valve dysfunction was noted in 2 cases and led to initial misinterpretations of the cause—as rheumatic heart disease[13] and atrial myxoma.[24] The results of cytologic study of effusions, given in 10 cases, suggest this to be an insensitive means of detecting tumor, since only 30% of these cases demonstrated malignant or atypical cells. The 20 cases in which the microscopic pattern of the tumor is reported reveal an even distribution over the 3 histologic variants of mesothelioma.

Pericardial mesothelioma is a highly lethal disease (Table IV). In 1 of the 28 cases, a possible cure was achieved by surgical excision of a discrete tumor mass attached to the parietal pericardium.[30] Com-

TABLE IV. Status of Patients at Time of Article's Publication*

Not available	1/28 (4%)
Dead of disease	24/27 (89%)
Alive with disease	2/27 (7%)
Alive without evidence of disease	1/27 (4%)

*Drawn from references 10 through 33 and the present case.

plete excision was not possible in the remainder of the patients, although partial excision was undertaken in a number of cases. This appeared to be of temporary benefit in selected patients.[14,22,27,31] Chemotherapy and radiation therapy appear to be of little benefit in cases of non-resectable tumor.[24,28-30,32] In 20 fatal cases, the time course of disease was documented and the patients lived an average of 3.5 months after presentation or initiation of therapy.

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